## **CLAIMS**

- 1. An isolated and purified nucleic acid encoding a GRK4 protein having an R65L, A142V mutation, an R65L, A486V double mutation, or an R65L, A142V, A486V triple mutation.
- 2. An oligonucleotide which specifically hybridizes to a *GRK4* gene having a sequence that encodes an R65L mutation, an A142V mutation, an A486V mutation, an R65L, A142V double mutation, an R65L, A486 double mutation or an R65L, A142V, A486V triple mutation.
- 3. An oligonucleotide primer which hybridizes to exon 3, 5, 8, 14 or 16 of a *GRK4* gene, and is useful in amplifying a DNA sequence including nucleotides 431 to 503 (exon 3), 594 to 697 (exon 5), 857-995 (exon 8), 1662 to 1798 (exon 14), and 1937 to 1991 (exon 16) of said gene.
- 4. A method of identifying individuals predisposed to essential hypertension, comprising:

obtaining kidney cells having a D1 receptor and expressing GRK4 from said individual; and

assaying said cells to determine extent of post-translational modification of said D1 receptor, wherein a change in post-translational modification of said D1 receptor relative to extent of post-translational modification of a D1 receptor in kidney cells having a D1 receptor and expressing *GRK4* isolated from a normotensive individual, is indicative of a predisposition to essential hypertension.

- 5. The method of claim 4, wherein said cells are assayed for the extent of palmitoylation of said D1 receptor.
- 6. The method of claim 4, wherein said cells are assayed for the extent of phosphorylation of said D1 receptor.
- 7. The method of claim 4, wherein said cells are assayed for hyperphosphorylation of said D1 receptor.
- 8. The method of claim 4, wherein said kidney cells are renal proximal tubule cells or cortical duct collecting cells.
- 9. A reconstituted system that measures GRK activity, comprising GRK4 and a GRK4 substrate.

- 10. The reconstituted system of claim 9, wherein said GRK4 substrate is a D1 receptor or a functional fragment thereof.
- 11. The reconstituted system of claim 10 which is a whole cell that expresses said GRK4 and said GRK4 substrate.
- 12. The reconstituted system of claim 11, wherein said whole cell is a Chinese hamster ovary cell transfected with a first heterologous gene encoding a D1 receptor and a second heterologous gene encoding a GRK4 protein associated with hypertension.
- 13. The reconstituted system of claim 9, wherein said GRK4 protein is associated with essential hypertension.
- 14. A complex between a GRK4 protein associated with hypertension and an agent which provides a detectable conformational change in said GRK4 protein upon interaction with a substance being analyzed for anti-hypertensive activity.
  - 15. An immortalized human proximal tubular cell.
- 16. An isolated and purified renal proximal tubular cell obtained from a hypertensive human.
- 17. The isolated and purified renal proximal tubular cell of claim 16, which is immortalized.
- 18. A transgenic animal, comprising a diploid genome comprising a transgene encoding a GRK4 protein which is expressed in renal cells to produce said GRK4 protein, and wherein expression of said transgene causes said transgenic animal to exhibit a state of essential hypertension compared to a normotensive animal whose renal cells do not express said GRK4 protein.
- 19. The transgenic animal of claim 18, wherein said renal cells have a decreased ability to reject sodium compared to a normotensive animal whose renal cells do not express said GRK4 protein.
  - 20. The transgenic animal of claim 18, which is a rodent.
  - 21. The transgenic animal of claim 18, which is a mouse.
- 22. A method of identifying putative anti-hypertensive agents, comprising: adding at least one candidate agent to the reconstituted system of claim 9; and detecting GRK4 activity, wherein a change in said activity is indicative of a putative anti-hypertensive substance.

- 23. The method of claim 22, wherein said step of detecting GRK4 activity comprises measuring adenylyl cyclase activity.
- 24. The method of claim 22, wherein said step of detecting GRK4 activity comprises adding a substrate to which phosphate can be added, and a phosphate source to said culture, and measuring phosphorylation of said substrate.
  - 25. A method of identifying putative anti-hypertensive agents, comprising:

contacting at least one candidate agent with the complex of claim 14, and detecting whether a conformational change in said GRK4 occurs, wherein a conformational change is indicative of putative anti-hypertensive activity.

- 26. The method of claim 25, wherein said detecting is conducted by spectrophotometry, fluorescence, nuclear magnetic resonance, evanescent wave technology or atomic force microscopy.
  - 27. A method of identifying putative anti-hypertensive agents, comprising:

adding at least one candidate agent to a culture of immortalized kidney cells that express a D1 receptor and GRK4 isolated from a hypertensive animal; and

detecting a change in transduction of a dopaminergic signal in said cells, wherein a change in transduction of a dopaminergic signal is indicative of putative anti-hypertensive activity.

- 28. A method of identifying putative anti-hypertensive agents, comprising:
- comparing electrolyte output of a first transgenic animal of claim 18 administered said agent, and a second transgenic animal of claim 18 not administered said agent, whereby a putative anti-hypertensive agent is identified by increased electrolyte output of said first transgenic animal as compared to said second transgenic animal.
- 29. A method of increasing natriuresis, comprising administering to an essential hypertensive individual a drug that interacts with GRK4 so as to increase natriuresis insaid individual.
- 30. The method of claim 29, wherein said drug changes expression of *GRK4* in kidney cells of said hypertensive individual.
- 31. The method of claim 29, wherein said drug comprises antisense RNA that binds *GRK4* mRNA or DNA.
- 32. The method of claim 29, wherein said drug comprises a ribozyme that cleaves *GRK4* mRNA or pre-mRNA.

- 33. The method of claim 29, wherein said drug comprises a dominant negative mutant DNA molecule.
  - 34. The method of claim 29, wherein said drug binds GRK4 protein.
- 35. An oligonucleotide which specifically hybridizes to *GRK4* mRNA *in vitro* or *in vivo*.
  - 36. The oligonucleotide of claim 35, which is an antisense RNA molecule.
- 37. The oligonucleotide of claim 35, which is a dominant negative mutant DNA molecule.
  - 38. A ribozyme that cleaves GRK4 mRNA or pre-mRNA.